Research Article

Formulation and Evaluation of Orodispersible Film of Hyoscine Butylbromide

Vineetha K*, Shetty S K, Prasad S N, Shivani, Kothwal S, Shenoy S, Shabaraya A R
Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Farangipete Post, Mangalore-574143, Karnataka, India.
***Corresponding author's E-mail:** kvineetha8@gmail.com

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ABSTRACT

Orodispersible film is a newly advancing novel drug delivery dosage form, which is useful for the patients who are bedridden. It has the most advantages over the other dosage forms such as tablets, capsules etc. The objective of this study was to design and optimize ODFs for improved drug delivery. The orodispersible films were formulated using Hyoscine Butylbromide, HPMC E5, HPMC E15, β-Cyclodextrin, Sodium saccharin, PVP-400. The evaluation of ODFs encompasses various aspects, such as weight variation which was observed to be in the range of 0.030 ± 0.007mg to 0.064 ± 0.0181 mg, thickness which was in the range of 0.0116 ± 0.0028 to 0.02 ± 0.01 mm for the 4 formulation, Folding endurance had a range of 95 ± 1.0 to 110 ± 2.0 folds, the surface pH range was found out to be 6.03 ± 0.69 to 6.48 ± 0.50. The drug content displays a variation between 66.58 ± 0.87% to 76.56 ± 3.53%. Orodispersible films were disintegrated at a time ranging from 25 ±1 seconds to 32 ± 2 seconds. The *in vitro* dissolution of four formulations study revealed a variance ranging from 41.63 ± 0.776 to 88.7 ± 1.41% at 180 seconds. Upon analysing the four formulations that were prepared, it was determined that F2 exhibited a more rapid dissolution time, lower weight variation, faster disintegration time, and possessed an appropriate thickness.

Keywords: Orodispersible film, Hyoscine Butylbromide, Solvent Casting Method, HPMC.

INTRODUCTION

Chronic abdominal pain is a common gastrointestinal (GI) symptom that characterizes many functional GI disorders/disorders of gut-brain interaction, including irritable bowel syndrome, functional dyspnoea, and centrally mediated abdominal pain syndrome. The symptoms of abdominal pain in these highly prevalent disorders are often treated with antispasmodic agents. Antispasmodic treatment includes a broad range of therapeutic classes with different mechanisms of action, including anticholinergic/antimuscarinic agents, calcium channel inhibitors and direct smooth muscle relaxants.[1]

Hyoscine N-Butylbromide (HNB) is a quaternary ammonium compound with an anticholinergic effect and is commonly used as an antispasmodic drug. HNB decreases motility in the gastrointestinal and genitourinary systems by blocking acetylcholine at the parasympathetic nerve endings of smooth muscle and secretory glands. HNB preparations (Buscopan®) have been used in the symptomatic treatment of spasmodic pain of these systems without a prescription in many countries.[2]

Despite tremendous innovations in drug delivery, the oral route remains the preferred route for the administration of therapeutic agents because of accurate dosage, low-cost therapy, self-medication, non-invasive methods and ease of administration leading to a high level of patient compliance. However, traditional tablets and capsules administered with a glass of water may be inconvenient or impractical for some geriatric patients because of changes in various physiological and neurological conditions associated with aging including difficulty in swallowing/dysphagia, hand tremors, deterioration in their eyesight, hearing, memory, risk of choking in addition to change in taste and smell.[3]

Fast-dissolving dosage forms have gained popularity and acceptance recently as new drug delivery systems due to their unique properties as they quickly disintegrate and dissolve in the mouth and can be administered without water, making them particularly suitable for patients. Fast-dissolving dosage forms include tablets, films, and microspheres. Tablets are the most commonly used among them.[4]

Fast dissolving tablets (FDTs) are also known as fast disintegrating/melting tablets, whereas orodispersible films are stamp-sized polymeric thin sheets that rapidly disintegrate in the mouth upon contact with saliva, without the need for additional fluid. Orodispersible films have advantages over tablets, that is their disintegrating time is faster than tablets[5]. Orodispersible films can be formulated easily and can be stored in aluminium foil. Orodispersible films have a larger surface area to dissolve when compared to Orodispersible tablets.[6,7]

Orodispersible films (ODFs) are ultra-thin, stamp-sized, elegant, portable, and patient-centric pharmaceutical dosage forms that do not need water to be ingested. They are particularly useful for paediatric and geriatric patient populations with special needs such as dysphagia, Parkinson's disease, and oral cancer and require careful consideration of both patient and dosage form factors including swallowability, palatability, and administration.[8]

The purpose of this study was to formulate orodispersible films of Hyoscine Butylbromide to provide immediate onset of action by releasing the drug at a faster rate, for achieving

improved oral bioavailability in shorter period of time and enhance patient compliance.

MATERIALS AND METHODS

Materials

Hyoscine Butylbromide was supplied from Yarrow Chem Products, Mumbai. All other excipients and solvents used were of the analytical pharmaceutical grade.

Methods

Formulation of orodispersible films

Solvent Casting Method:[9, 10]

The required quantity of film-forming polymer was dissolved in 20 ml distilled water which was taken in a beaker. Polymer was dissolved uniformly with the help of a magnetic stirrer which was maintained at 400 to 600 rpm. Once the polymer was dissolved, the other excipient was added to a polymer solution in an increasing order of weight. After the solution was prepared, the solution was checked for air bubbles. The pre-measured petri dish was kept in a hot air oven and then solution was poured into it. Petri dishes should not be in an elevated position on one side, to avoid non-uniform drug distribution. Hot air oven was maintained at a temperature of 60 ºC for a period of 6-7hrs. Once the prepared film was dried, then film was cut into 2cm×2cm and evaluation studies were carried out.

Calculation of the amount of drug for one cast film:

- Internal diameter of Petri dish = 9cm
- Radius of Petri dish = 4.5cm
- Internal surface area of petri dish = πr2

  = 22/7 × (4.5)2 = 63.64cm^2
- Surface area of strip = 2cm×2cm = 4 cm^2
- 4cm^2 contains 10mg
- 63.64cm^2 contains = 70.71grams

Table 1: Formulation chart for the preparation of Orodispersible Film

Ingredients	Formulations (mg)			
	F1	F2	F3	F4
Hyoscine Butylbromide	71	71	71	71
HPMC E5	200	400	-	-
HPMC E15	-	-	200	400
β-Cyclodextrin	100	100	100	100
Citric acid	70	70	70	70
Sodium Saccharine	10	10	10	10
PVP 400	0.2ml	0.2ml	0.2ml	0.2ml
Distilled water	20ml	20ml	20ml	20ml

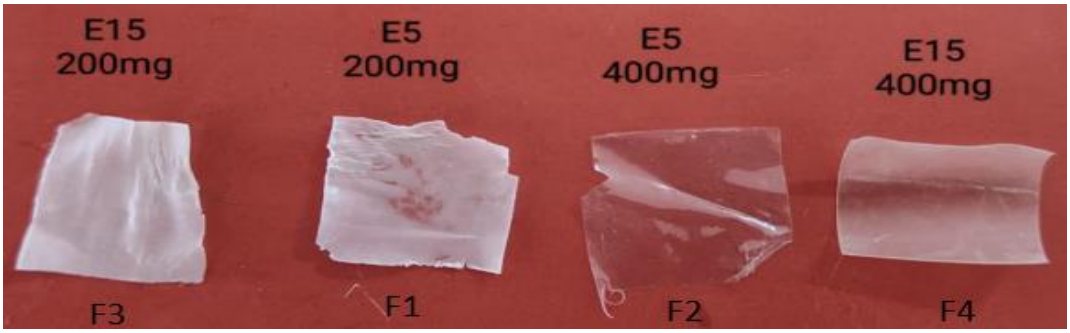

Figure 1: Formulation of ODF

Evaluation of orodispersible films:

1. Weight variation:[11]

4 individual batches of fast dissolving film of size 2×2 cm^2 were cut and weighed on electronic balance for weight variation test.

2. Film Thickness:[12]

Uniformity in the thickness helps in the understanding of the drug uniformity in the ODFs and Drug dose. Micrometer screw gauge was used to find the thickness of the ODF (2cm × 2cm). Thickness was measured at different corners and also at the centre of the film.

3. Determination of pH:[13]

The film of 2cm×2cm was taken in a petri dish (or in a beaker) and 10 ml of phosphate buffer (pH 6.8) was taken. Then the film was dissolved in a beaker and pH was determined.

4. Folding endurance:[14]

The films of 2cm×2cm were subjected to multiple folding until cracks became visible. Subsequently, a thorough examination of the films was conducted to identify any cracks. In the event that cracks were detected, the number of folds leading to their appearance was recorded, along with the corresponding standard deviation.

5. Drug content:[15]

Films were placed in a 100 ml volumetric flask and dissolved in phosphate buffer pH 6.8 solutions. The contents were stirred with a magnetic stirrer to dissolve the films and the volume was completed then filtered through Whattman filter paper, to separate out the insoluble excipient. The absorbance of the solution was

measured at 212 nm against the corresponding blank. In the case of HPMC films, distilled water was used to dissolve the film and then suitably diluted phosphate buffer pH 6.8. The estimations were carried out in triplicate.

6. Disintegration time:[16]

Disintegrating time is defined as the time at which film breaks when it is brought in contact with water or saliva. In this method 2 ml phosphate buffer was placed in a petri dish and one film was added on the surface of the phosphate buffer and the time is measured until the film was dissolved completely.

7. *In vitro* Dissolution:[17]

The optimized films, which had a known weight and dimension of 2 × 2 cm, were immersed in a beaker containing 20 ml of phosphate buffer with a pH of 6.8. This fluid served as the dissolution medium and was maintained at a temperature of 37±0.5°C. To ensure uniform mixing, the medium was stirred at a speed of 50 rpm.

At regular intervals of 5 seconds, aliquots of 5 ml were withdrawn from the beaker and replaced with an equal volume of fresh phosphate buffer. The withdrawn samples were then filtered, suitably diluted, and subjected to analysis using a UV/Visible spectrophotometer (V-630, JASCO, Japan) at a wavelength of 212 nm, which corresponded to the maximum absorbance of the drug.

The cumulative percentage of drug release was calculated based on the absorbance values obtained and plotted against the corresponding time in seconds.

RESULTS AND DISCUSSION

Table 2 (a): Evaluation of orodispersible film of Hyoscine Butylbromide

Formulation Code	Weight Variation (mg) *	Thickness (mm) *	Surface pH*
F1	0.031 ± 0.0103	0.0166 ± 0.0057	6.03 ± 0.69
F2	0.030 ± 0.007	0.0116 ± 0.0028	6.48 ± 0.50
F3	0.064 ± 0.0181	0.0133 ± 0.0057	6.33 ± 0.83
F4	0.044 ± 0.0089	0.02 ± 0.01	6.24 ± 0.19

*Data expressed as mean ± SD, n=3

Table 2(b): Evaluation of orodispersible film of Hyoscine Butylbromide

Formulation code	Folding Endurance (No. of Folds) *	Drug content (%) *	Disintegration Time (in seconds) *
F1	95 ± 1	71.46 ± 1.73	32 ± 2
F2	110 ± 2	76.56 ± 3.53	25 ±1
F3	104.6 ± 1.52	66.58 ± 0.87	28 ± 2
F4	108.6 ± 2.51	69.60 ± 0.83	29 ± 1

*Data expressed as mean ± SD, n=3

1. Weight variation:

The weight of prepared films was determined using digital balance and an average weight of all films is given in table no.2(a). All the films passed the weight variation test as the standard deviation of percentage weight variation of individual formulations was within pharmacopeial limits of 7.5%. It was found to be in the range of 0.030 ± 0.007 mg to 0.064 ± 0.0181 mg.

2. Film thickness:

The thickness of fast-dissolving film depends on the concentration of the polymer. The thickness of all fast-dissolving films was measured with a micrometer screw gauge. The thickness of the films F1 to F4 varies from 0.0116 ± 0.0028 mm to 0.02 ± 0.01 mm with low standard deviation values. Formulation F2 showed the lowest thickness of 0.0116 ± 0.0028 mm and F4 showed the highest thickness of 0.02 ± 0.01 mm.

3. Surface pH:

The surface pH of the films F1 to F4 was ranging from 6.03 ± 0.69 to 6.48 ± 0.50 as shown in table No.2(a). The surface pH of all the films was uniform and within the range of 5.5 – 6.5.

4. Folding Endurance:

All the films were subjected to folding endurance. The formulation F2 showed a folding endurance of 110 ± 2 folds which is greater than other three formulations. This maybe because of higher concentration of the polymer, HPMC E5.

5. Drug content:

Drug content of the formulation was found in the range of 66.58 ± 0.87 to 76.56 ± 3.53 within the required range. F2 showed highest drug content of 76.56 ± 3.53 in the film.

6. Disintegration Time:

All the films are disintegrated rapidly. The formulation F2 showed the lowest disintegration time of 25 ±1 seconds indicating quicker disintegration.

7. *In vitro* Dissolution:

All the films were subjected to *in vitro* dissolution studies and the formulation F2 showed a greater drug release of 88.7 ± 1.41 within 180 sec which was quicker than that of the other 3 formulations.

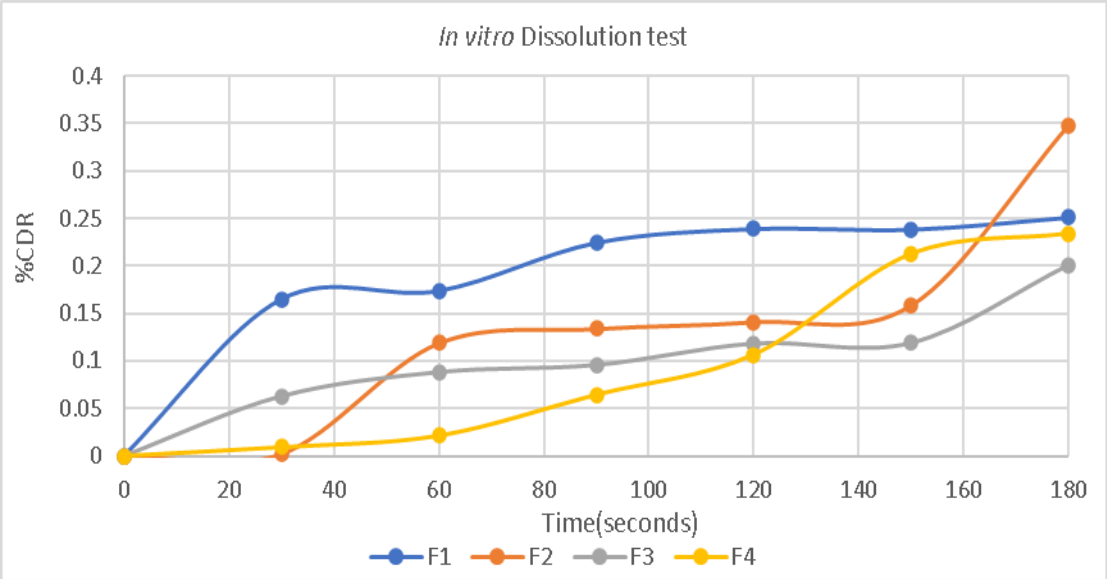

Figure 2: *In vitro* Dissolution Studies of Hyoscine Butylbromide

CONCLUSION

In the present research work orodispersible films of Hyoscine butyl bromide were formulated by solvent casting method using HPMC E 5 and HPMC E 15 polymer combination for abdominal cramping and pain. The prepared formulations were evaluated using different parameters and they exhibited acceptable physical characteristics with good flexibility, thickness and folding endurance. All the formulations quickly disintegrated and released the drug. Therefore, orodispersible films can be considered potentially suitable for the immediate release of drug Hyoscine butyl bromide for reducing abdominal cramps and pain.

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